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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,560	06/04/2001	Christopher M. Dobson	720797.90019	3009

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EXAMINER	
NICHOLS, CHRISTOPHER J	
ART UNIT	PAPER NUMBER
1647	12

DATE MAILED: 07/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,560	DOBSON, CHRISTOPHER M.	
	Examin r	Art Unit	
	Christopher Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1. 5 3 9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election **without** traverse of Group I (claims 38-52) drawn to a process for preparing an amyloid fibril in Paper No. 11 (6 May 2003) is acknowledged.

Status of Application, Amendments, and/or Claims

2. The Preliminary Amendment filed 6 May 2003 (Paper No. 11) has been received and entered in full. Claim 53 has been cancelled.

3. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647, Examiner Christopher Nichols.

Priority

4. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed is not valid as it is drawn to a PCT filed in a foreign country.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims **38-51** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *a method for preparing an amyloid fibril as defined by claim 38 wherein the protein is selected from the group consisting of the SH3 domain of the p85α subunit of PI3-kinase, human muscle acylphosphatase, CspB-1, CspB-2, CspB-3, and wild type human carboxypeptidase A2 wherein the solution comprises an alcohol and acetonitrile or urea and wherein the non-naturally occurring amyloid fibril prepared by said method comprises a metal selected from the group consisting of copper, silver, or gold*, does not reasonably provide enablement for *any other proteins, other metals*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

6. The above invention is drawn to methods of preparing a non-naturally occurring amyloid fibril. The language of said claims encompasses all known and unknown proteins. The specification teaches that the SH3 domain of the p85α subunit of PI3-kinase, human muscle

acylphosphatase, CspB-1, CspB-2, CspB-3, and wild type human carboxypeptidase A2 can be used to practice the method with results hinging on the time of incubation, pH, temperature, and protein concentration.

7. Since the specification fails to provide any guidance for the successful use of other proteins and since resolution of the various complications in regards to amyloid fibril formation versus aggregation with fibrils (such as a neurofibrillary tangle) is highly unpredictable, one of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the prior art as outlined above, the quantity of experimentation required to practice the invention as claimed to its *full scope* would require the *de novo* determination of formulations with known pH, protein concentration, solutes, solutions, temperature, and time to correlate with fibril formation. In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

8. The specification as filed does not provide any guidance or examples that would enable a skilled artisan to use the disclosed method of making a non-naturally occurring amyloid fibril from any protein. Additionally, a person skilled in the art would recognize that predicting the efficacy of using the method to make any protein into an amyloid fibril based solely on a few examples is highly problematic. Thus, although the specification prophetically considers and discloses general methodologies of using the other proteins, such a disclosure would not be considered enabling since the state of protein aggregation is highly unpredictable. The factors listed below have been considered in the analysis of enablement:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

9. The following references are cited herein to illustrate the state of the art of amyloid fibrils and amyloid proteins. Respecting the state of the prior art, Burdick *et al.* (5 January 1992) "Assembly and Aggregation Properties of Synthetic Alzheimer's A4/β Amyloid Peptide Analogs." The Journal of Biological Chemistry **267**(1): 546-554 teaches that pH, peptide concentration, and time of incubation as well as the length and nature of the protein used in the aggregation (fibril formation process) are critical for successful formation of fibrils (Table 1; Figures 3 and 4). Thus the skilled artisan is not given sufficient guidance in the instant Specification to practice the claimed invention to its full scope.In light of the nature of the instant invention, Sipe (1992) "Amyloidosis" Annu. Rev. Biochem. **61**:947-975 teaches that amyloid fibrils share a common ultrastructure of 7-10 nm wide, rigid, nonbranching fibrils of variable length (pp. 954). While Sipe (1992) is not exhaustive it does specify conditions, folding structures (β-pleated sheets), and size characteristics which define an "amyloid fibril". Thus the skilled artisan is presented with an undue burden of experimentation to practice the full scope of the instant invention which includes all proteins not just those known in the prior art or taught in the instant Specification to form amyloid fibrils.On the breadth of the claims, Perutz *et al.* (16 April 2002) "Amyloid Fibers are water-filled nanotubes." PNAS **99**(8): 5591-5595 teaches that β-amyloid forms narrow tubes (nanotubes) with a central water-filled cavity (Table 1; pp. 5595).

It is noted by Perutz *et al.* (2002) that it may be physically impossible for other aggregating or amyloid–like protein such as huntingtin to form such "amyloid fibrils"(pp. 5594). Therefore, not all proteins can be used to satisfy the preamble of claim 38.Further on the predictability of the art, Chiti *et al.* (March 1999) "Designing conditions for in vitro formation of amyloid protofilaments and fibrils." PNAS **96**: 3590-3594 teaches that with sufficient experimentation protein crystals can be formed in vitro in amyloid fibrils from proteins that do not generally form amyloid fibrils (pp. 3590). However Chiti et al. (1999) note that: "It is important to make it clear that the particular conditions we have used are not suggested to be universally appropriate for fibril formation by proteins." (pp. 3593) Thus the skilled artisan is confronted with little predictability for the conditions under which the instant invention may be practiced to its full scope as protein crystallization is known to be a notoriously difficult and unpredictable art.Thus the specification of the instant application fails to provide adequate guidance for one of skill in the art to overcome the unpredictability and challenges of applying results from *in vitro* experiments to the full range of proteins claimed as exemplified in the references above.

15. Claims **39-42** and **49-50** are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the amounts or molar concentrations of the additives to the reaction solution as put forth in claim 38 (e.g. alcohols, acetonitrile, urea, metals).

16. Claim **38** is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

17. The term "acceptable" in claim 38 is a relative term which renders the claim indefinite. The term "acceptable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear from the instant Specification or the prior art as to what the metes and bounds of "acceptable" are for the instant invention.

18. Claim **51** is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 51 recites the limitations "functional groups" and "reactants" the metes and bounds of which are not clear.

19. Claim **52** is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

20. Claim **52** provides for the use of a non-naturally occurring amyloid fibril, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

21. Claim **52** is also rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Summary

22. Claims 38-52 are hereby rejected.

23. The following patents and patent application publications were found by the Examiner during the prior art search and are here made of note:

a. US 6569383 B1 (27 May 2003) Nelson *et al.*

b. US 5721106 (24 February 1998) Maggio *et al.*

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:00AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

CJN
July 11, 2003

Gary L. Kunz
GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600